Black Fungi and Ionizing Radiation

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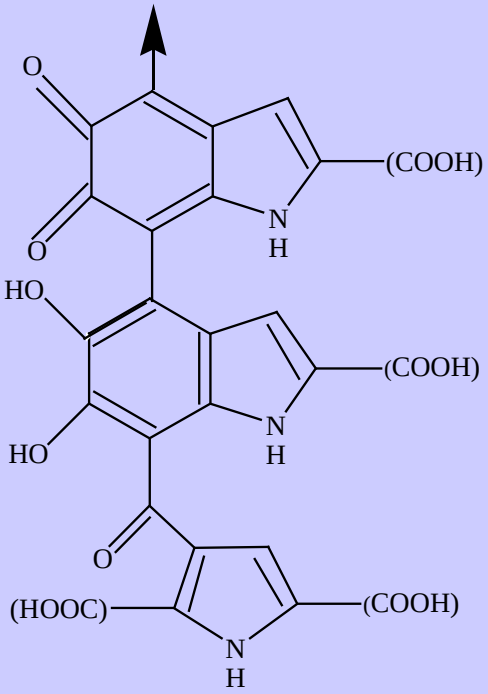
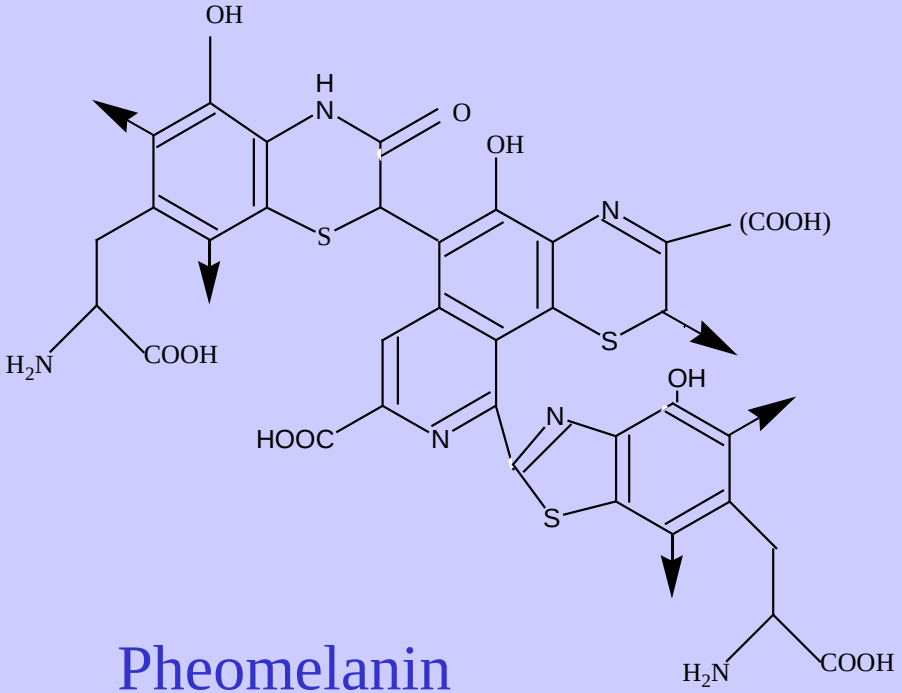
Background information on melanin and radiation

- Melanized microorganisms inhabit some remarkably extreme environments on the planet including high altitude, Arctic and Antarctic regions.
- Melanized fungal species colonize the walls of the damaged reactor at Chernobyl where they are exposed to a high constant radiation field.
- Cooling pool water in nuclear reactors is sometimes contaminated with melanized microorganisms.
- The laboratory observations of the resistance of melanized fungi to ionizing radiation.

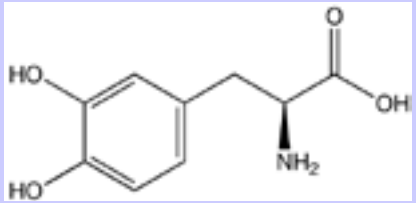
Melanin oligomers and pre-cursors

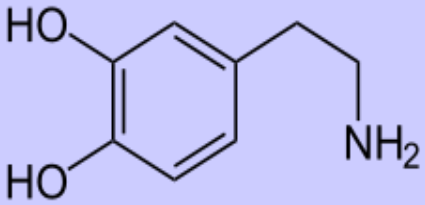


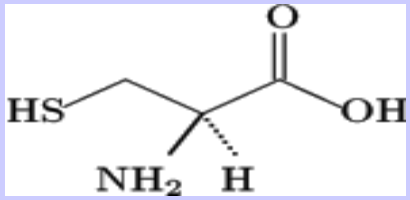
Eumelanin



Pheomelanin

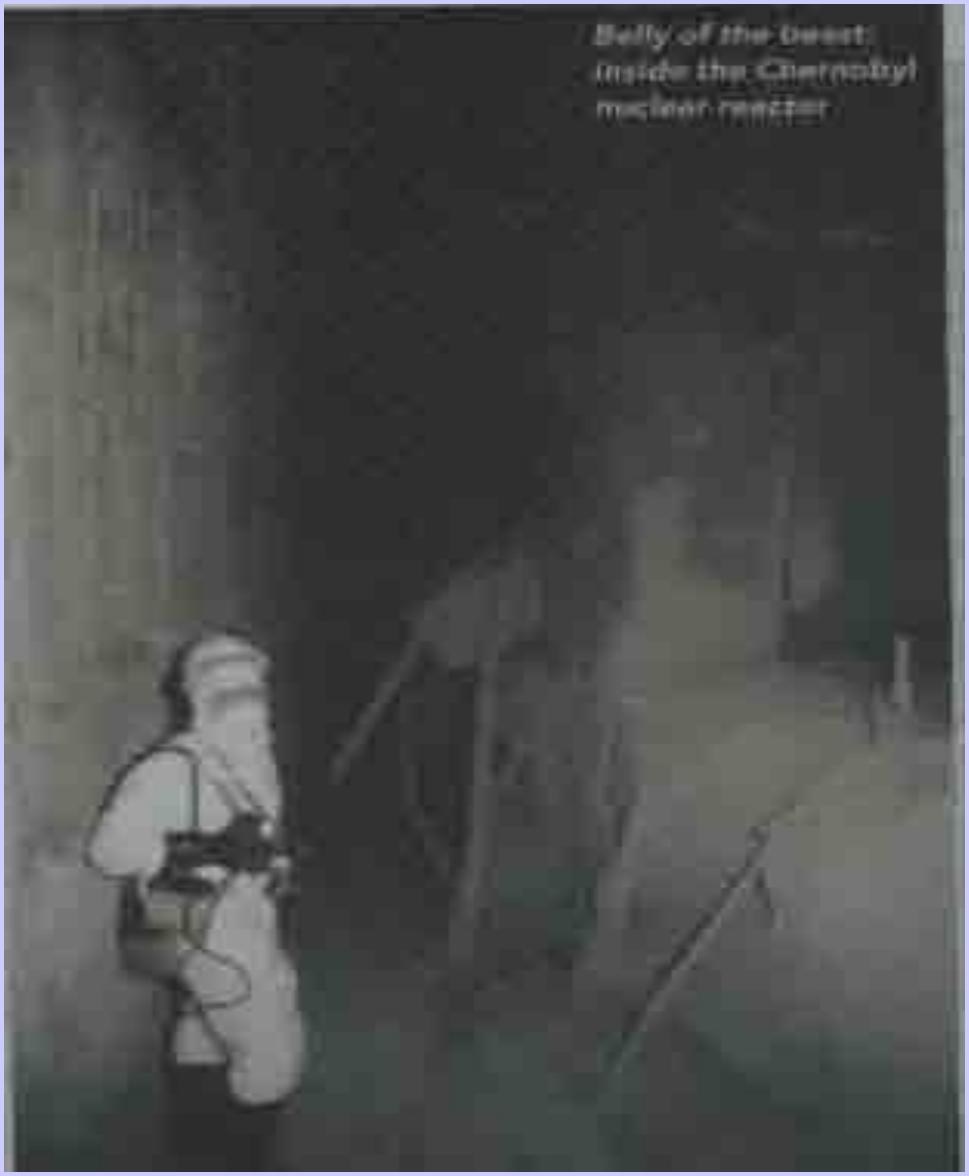




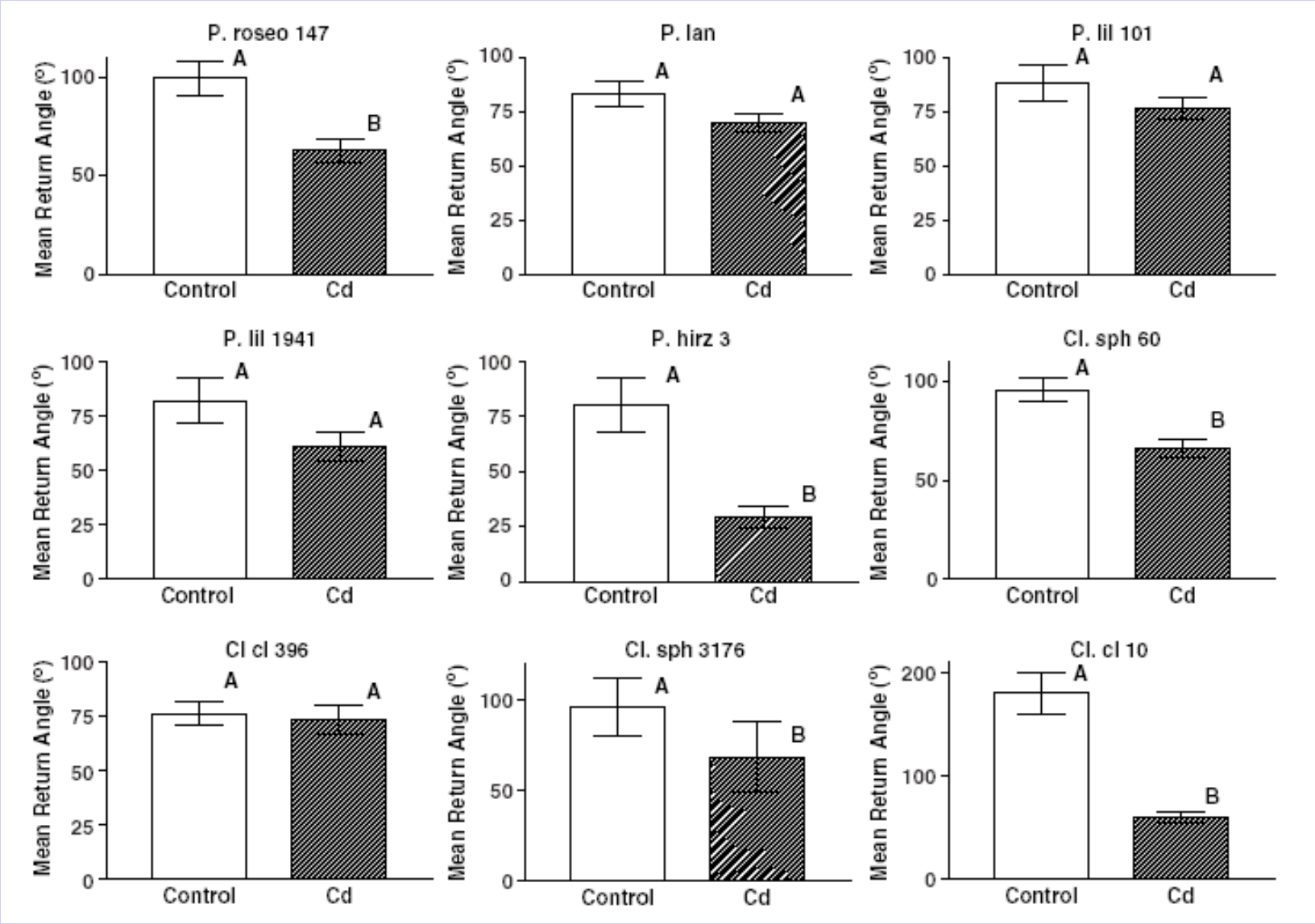


Melanin as an energy transducer in melanized fungi in radioactive environment

Inside Chernobyl reactor



Radiotropism of melanized fungi



Tugay T et. al. *Mycologia* 2006

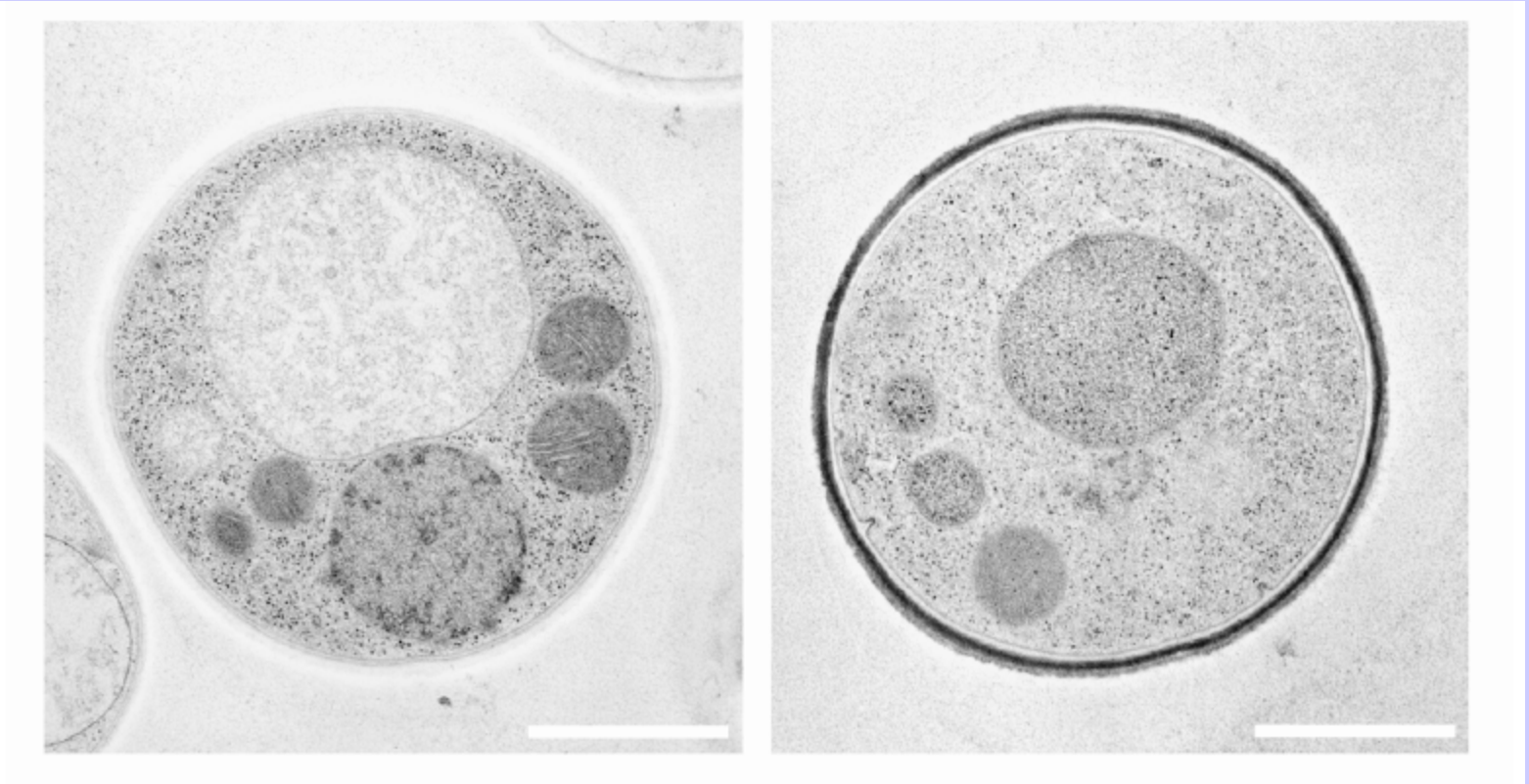
- Meredith and Sarna (2006) recently reviewed current state of knowledge in physico-chemical properties of melanin:
- optical properties
- condensed phase electric properties
- electron exchange
- paramagnetic
- ion exchange
- scattering of UV and visible radiation
- photoprotective and antioxidant properties
- HOWEVER,

No attempts to investigate the fundamental physics and chemistry of melanin interaction with ionizing radiation have been reported

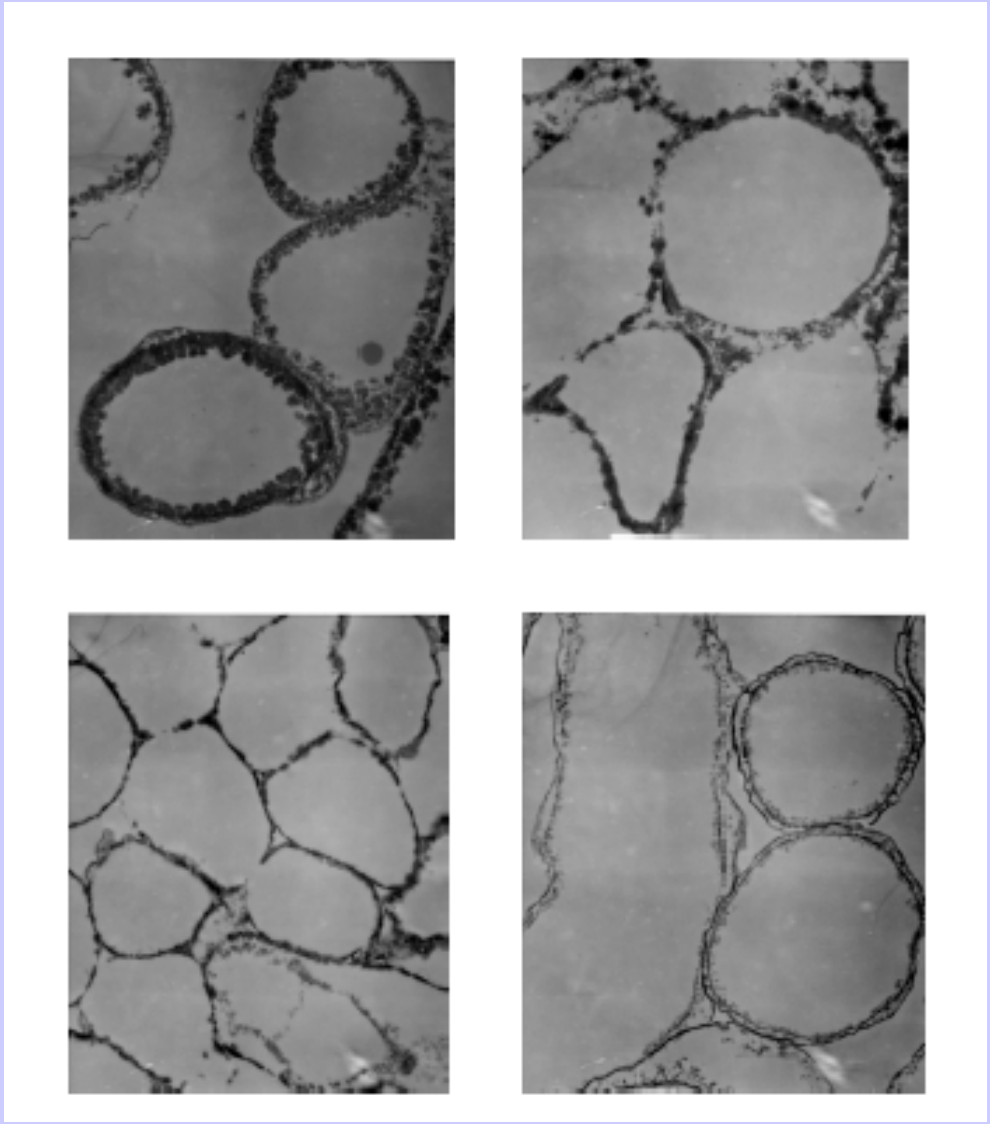
Hypothesis

In melanized fungi the energy of ionizing radiation is transduced into chemical energy which fungi can utilize in their life cycle.

Melanized and non-melanized *Cryptococcus neoformans*



Intrinsically melanized *Cladosporium sphaerospermum*



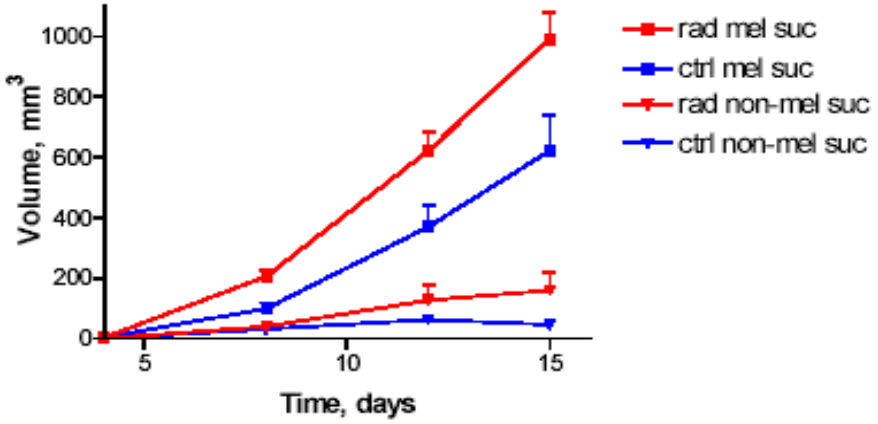
Melanin role as an electron shuttle is influenced by prior irradiation

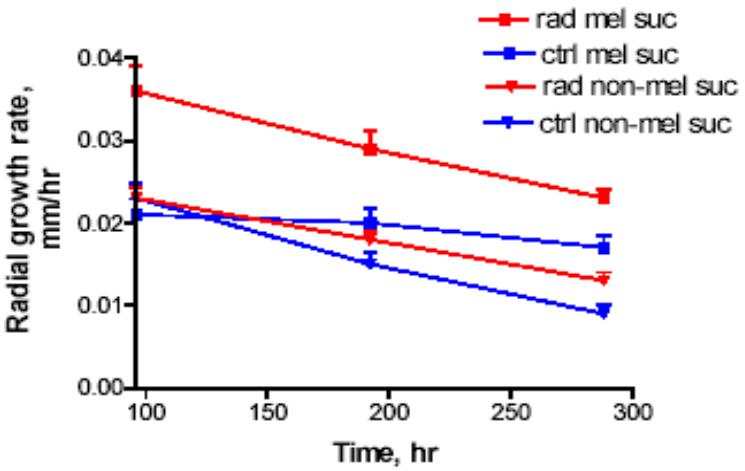
NADH-ferricyanide-melanin reaction in presence of untreated and irradiated *C. neoformans* melanin

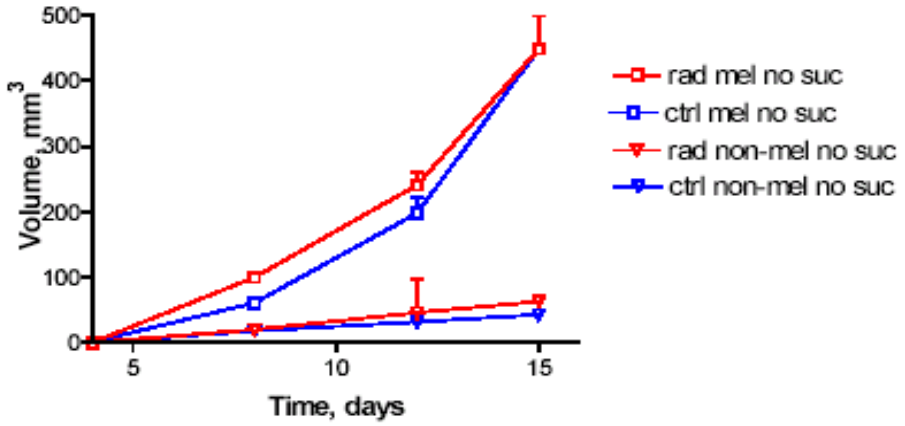
Sample	Reaction system		
	Ferricyanide + melanin	Ferricyanide + NADH + melanin	
	Ferricyanide reduced	NADH oxidized	Ferricyanide reduced
untreated melanin	40 nmol V^1 = 9 nmol/min	37 nmol	75 nmol V = 30 nmol/min
irradiated melanin, 20 min	60 nmol V = 13 nmol/min	100 nmol	200 nmol V = 80 nmol/min
irradiated melanin, 40 min	170 nmol V = 38 nmol/min	150 nmol	300 nmol V = 120 nmol/min

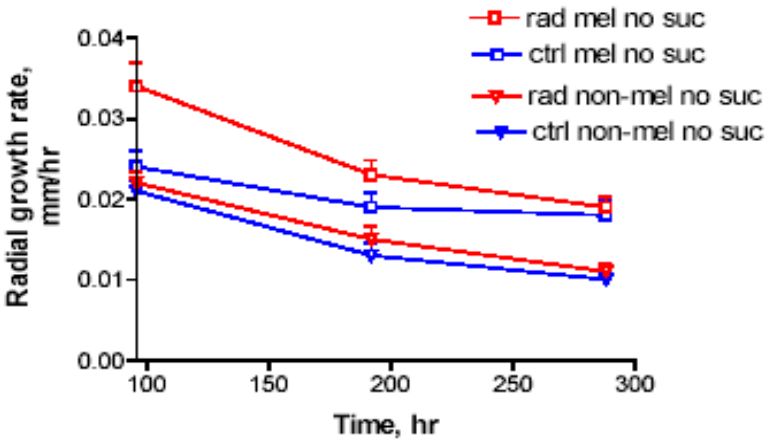
V - initial velocity is expressed in nanomoles of ferricyanide reduced per min.

Experiments with *C. sphaerospermum*

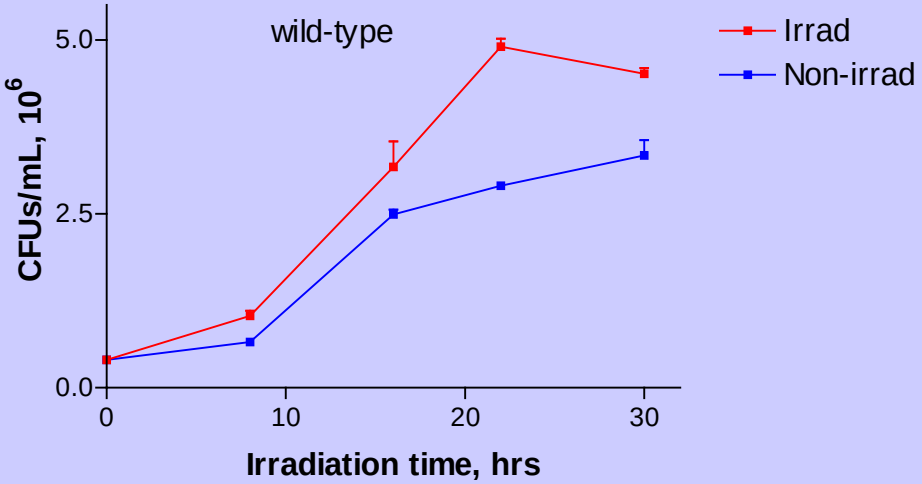


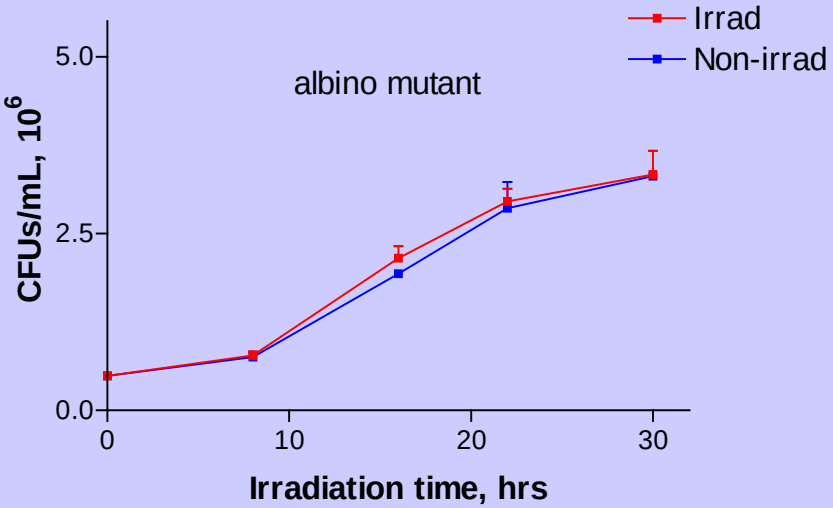


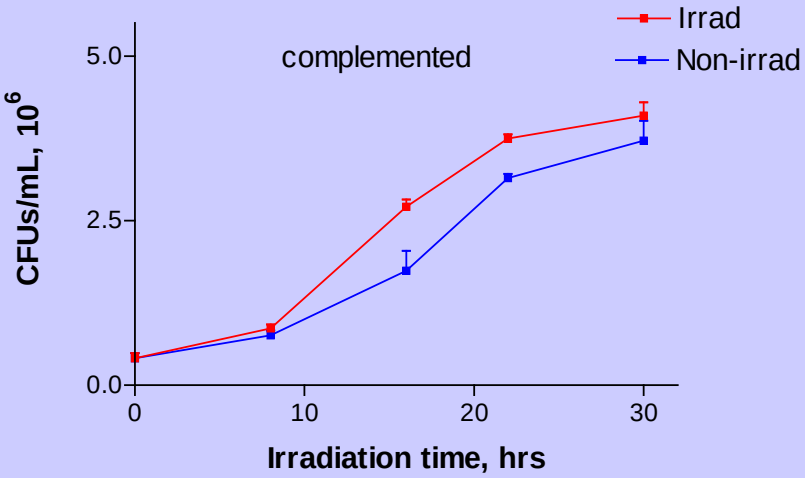


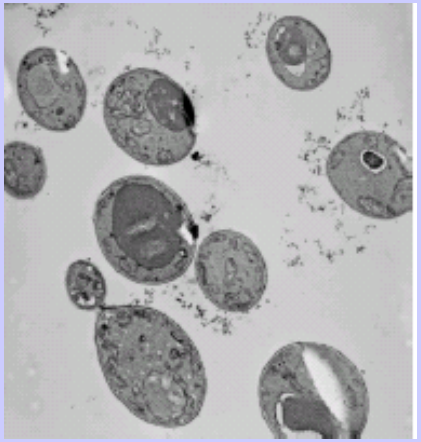


Experiments with *Wangiella dermatitidis*







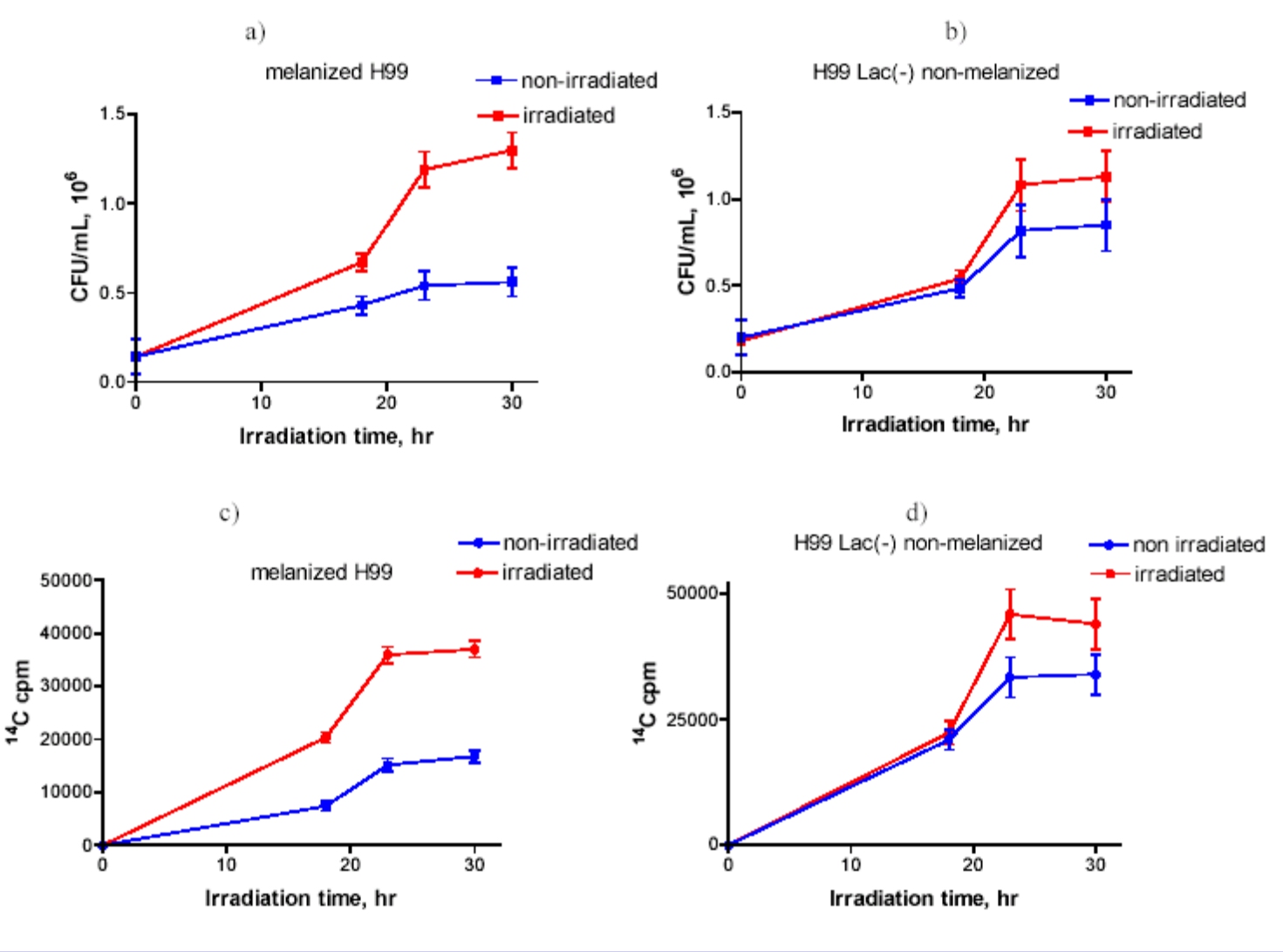


Doubling times for *W. dermatitidis*

strain	Doubling time, hr		
	irradiated	control	P value*
wild type	6.5 (0.1)	7.4 (0.2)	0.02
mutant	9.8 (1.0)	10.8 (1.8)	0.7
complemented	6.8 (0.1)	7.3 (0.1)	0.01

Doubling time = $\ln 2/((\ln(A/A_o)/t)$

Experiments with *C. neoformans*



Dadachova E, Bryan RA, Huang X, Moadel T, Schweitzer AD, Aisen P, Nosanchuk JD, and Casadevall A. PLoS One 2007, 5:e457

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Fungi Gobble Radiation to Grow, Study Says

By Scott Norris
for National Geographic News
May 22, 2007

Some fungi eat radiation to fuel their growth, a new study suggests.

Three species of fungi containing the black pigment melanin—a substance also present in human skin—grew larger and faster when exposed to high levels of radiation, even when deprived of nutrients.

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Week of May 26, 2007; Vol. 171, No. 21 , p. 325

Dark Power: Pigment seems to put radiation to good use

Davide Castelvecchi

Call them the Hulk bugs. Just as they do for the comic book hero, gamma rays seem to make certain microscopic fungi stronger. Researchers have found hints that melanin—the same pigment that's the natural ultraviolet filter in people's skin—might enable these fungi to harness the energy of gamma radiation as well as to shield themselves from it.

Science Friday
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Radiation-Eating Fungi / Biocomputers / Hurricane Forecast

One team of researchers has discovered fungi that "eat" radiation, in a

Colored fungi soak up the rays

Tue May 22, 2007 8:07pm ET

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By Maggie Fox, Health and Science Editor

WASHINGTON (Reuters) - Dark-colored fungi devour radiation and convert it to fuel, researchers said on Tuesday in a study that may offer applications from more efficient solar cells to feeding astronauts in space.

The study may also explain why it feels so good to soak up the sun on the beach, the researchers report in the Public Library of Science journal PLoS ONE.

News in science

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Fungus eats radiation for breakfast

Maggie Fox
Reuters

Wednesday, 23 May 2007

В Чернобыле обнаружены питающиеся радиацией грибы

Summary

•Melanin pigments are found in all biological kingdoms, suggesting that these compounds are ancient molecules that emerged early in the course of evolution.

•Melanins are complex polymers with a variety of properties that can be made enzymatically from relatively simple precursors. A remarkable aspect of melanins is their ability to absorb all types of electromagnetic radiation which endows them with the capacity for both energy transduction and shielding.

•The findings of melanized organisms in high radiation environments combined with phenomenon of 'radiotropism' raises the tantalizing possibility that melanins have functions analogous to other energy harvesting pigments such as chlorophylls.

Dadachova E. and Casadevall A. Curr. Opinion Microbiol. 2008

Potential applications of melanin's energy transduction properties

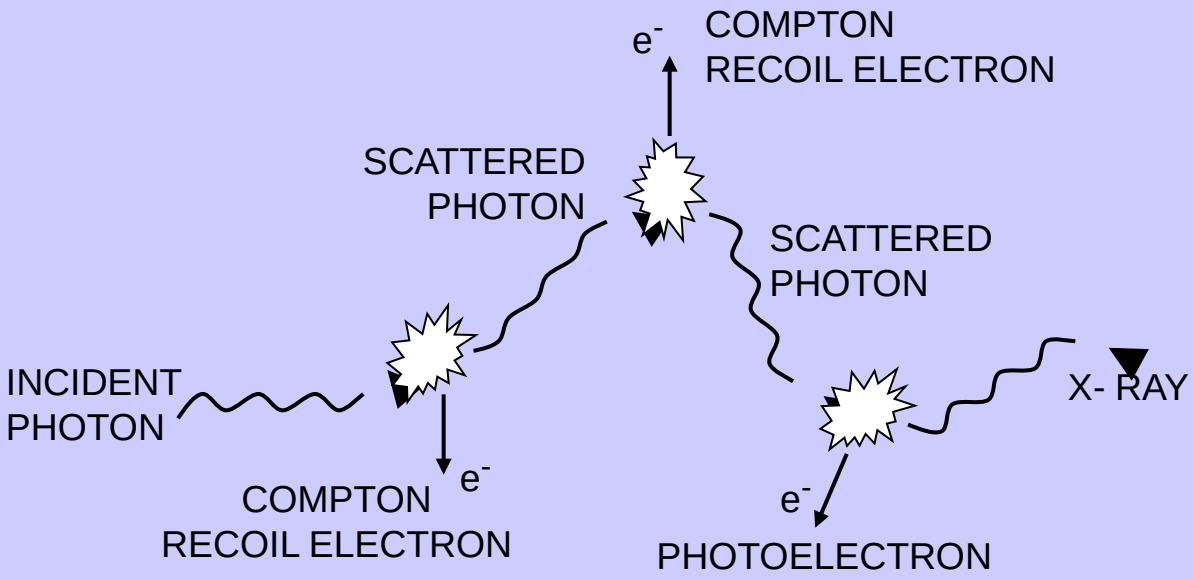
- Active bioremediation of soils contaminated with radionuclides
- Production of food by genetically modified plants using ionizing radiation as an energy source

On-going work

- Electrochemical investigation of fungal melanin interaction with ionizing radiation (PLOS ONE, submitted)
- Electron paramagnetic resonance (EPR) of live melanized cells interacting with ionizing radiation (PNAS, submitted)

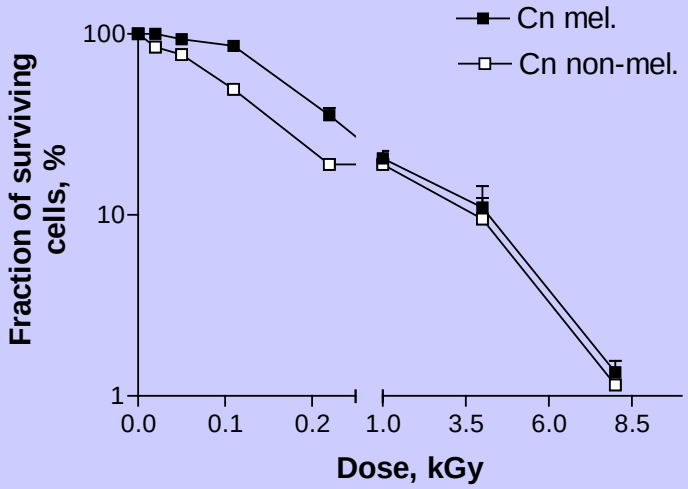
Melanized nanoparticles for protection of bone marrow from radiation during radiation therapy of cancer

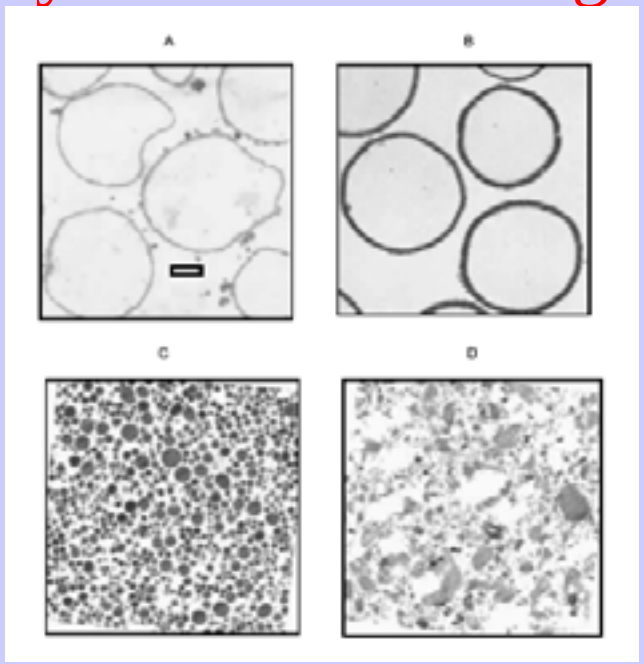
Diagram illustrating multiple interactions of a photon passing through matter

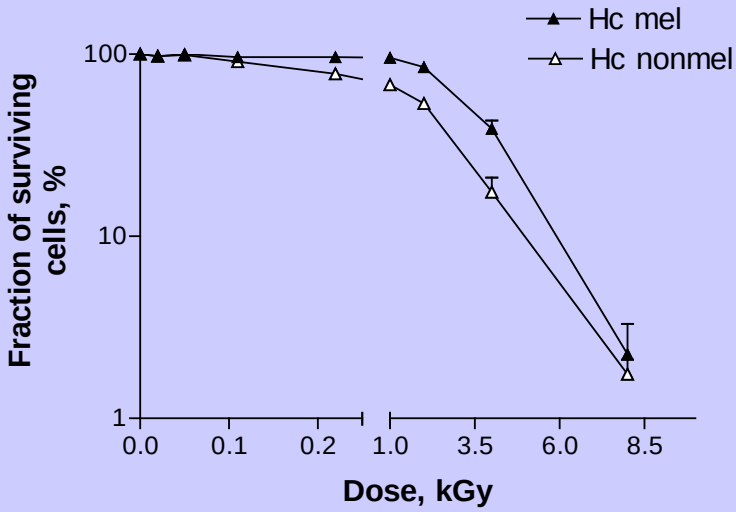


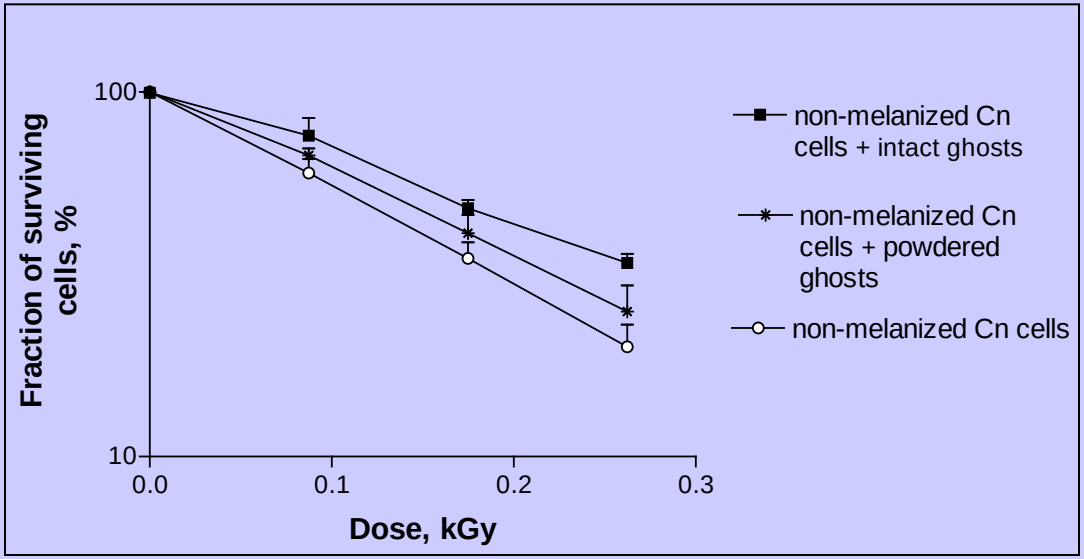
Our hypothesis - controlled dissipation of high-energy recoil electrons by melanin prevents secondary ionizations and the generation of damaging free radical species.

Protection of melanized cells by melanin from high doses of radiation









Physical proof of melanin radiation shielding properties

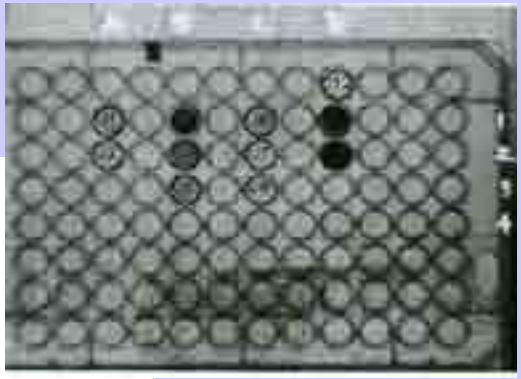


Table 1 Attenuation of diagnostic X-ray by suspensions of *C. neoformans* and Sepia melanin in comparison with non-melanin substances

		Internal pixel density (IPD) per mm^2		mean IPD/IPD(bkrd)	Attenuation (%)
	Amount, mg	1st	2nd (repeat)		
A Sepia melanin	**50**	1370	1370	1.12	**12**
	25	1280	1280	1.05	**5**
B *C. neoformans*	**100**	1720	1720	1.41	**41**
	50	1470	1470	1.21	**21**
	30	1346	1346	1.11	**11**
C Charcoal	**40**	1329	1329	1.09	**9**
	20	1248	1248	1.02	**2**
	15	1244	1244	1.02	**2**
D Lead foil	**100**	2202	2217	1.81	**81**
	200	2269	2277	1.87	**87**
Background	--	1218	1218	1	**0**

Dadachova E. et. al. Pigment Cell Melanoma Res. 2008

The need for radioprotectors in cancer treatment

- Half of all cancer patients in the US are undergoing radiation therapy in the course of their disease.
- Bone marrow is the dose limiting organ for many types of external beam radiation therapy (EBRT) and radioimmunotherapy (RIT).
- Protection of bone marrow before administering radiation treatment would increase the efficacy and safety of treatment.

How to deliver melanin to the bone marrow?

- Human body has a self-sieving effect directing particles in nanosize range to the bone marrow.

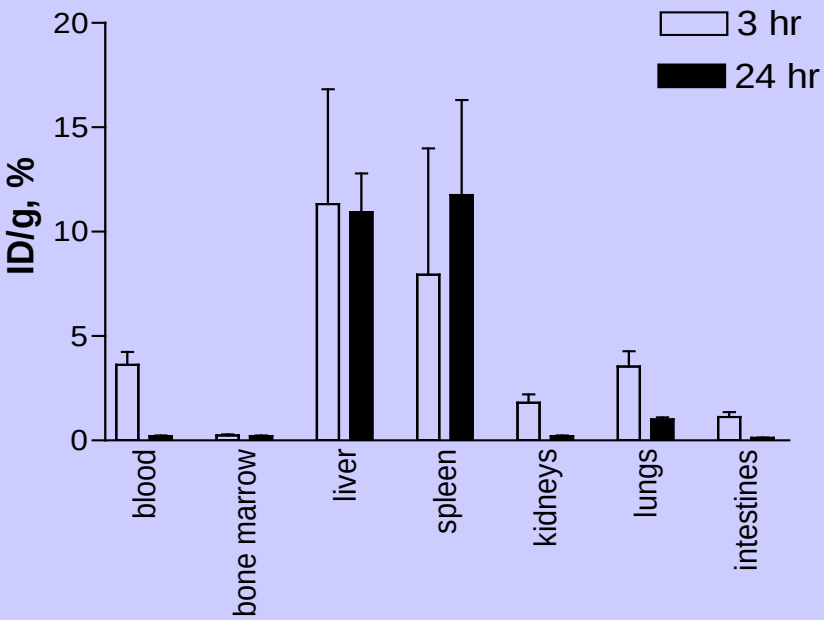
Bone marrow scan with 30 nm particles of ^{99m}Tc-sulfur colloid

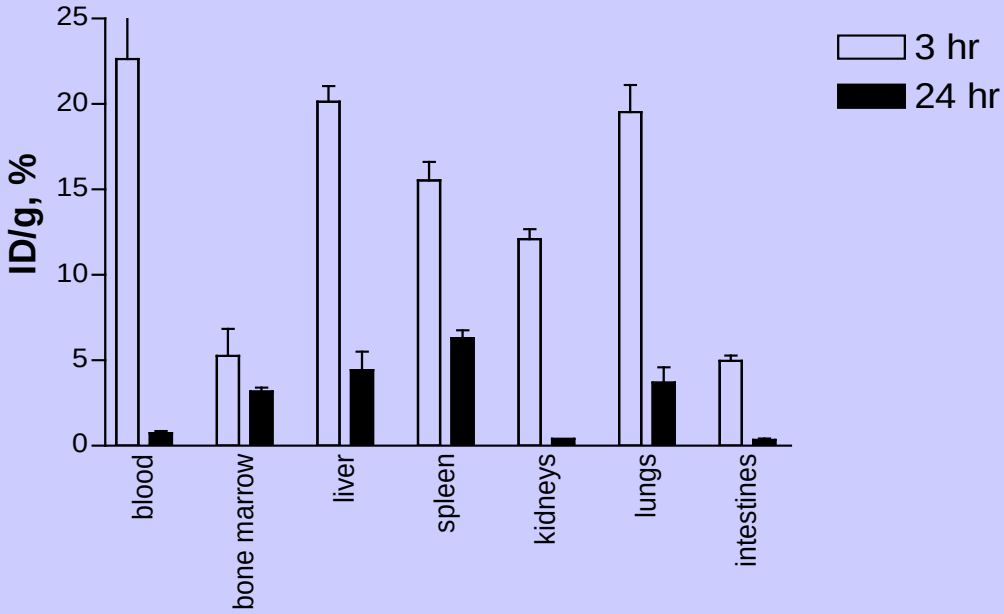
Characterization of synthetic melanins

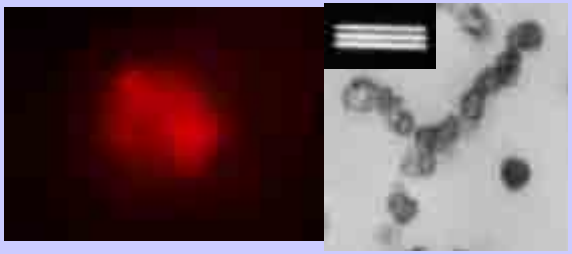
Melanin type	Precursors	Method of oxidation	%C	%H	%N	%S	Mass Attenuation Coefficient at 113 keV, cm^2/g	Number of stable free radicals (spins/g)
MEL1	Dopamine	Tyrosinase	48	3	7	N/D	0.154	1.26×10^{18}
MEL2	L-DOPA	Tyrosinase	52	4	7	N/D	0.155	9.05×10^{17}
MEL3b	L-Cysteine, L-DOPA	Tyrosinase	34	5	11	22	0.165	7.09×10^{18}
MEL4	5-S-cysteinyl-L-DOPA	Tyrosinase	46	4	9	10	0.157	2.14×10^{18}

Schweitzer AD et al. PLoS One, 2009

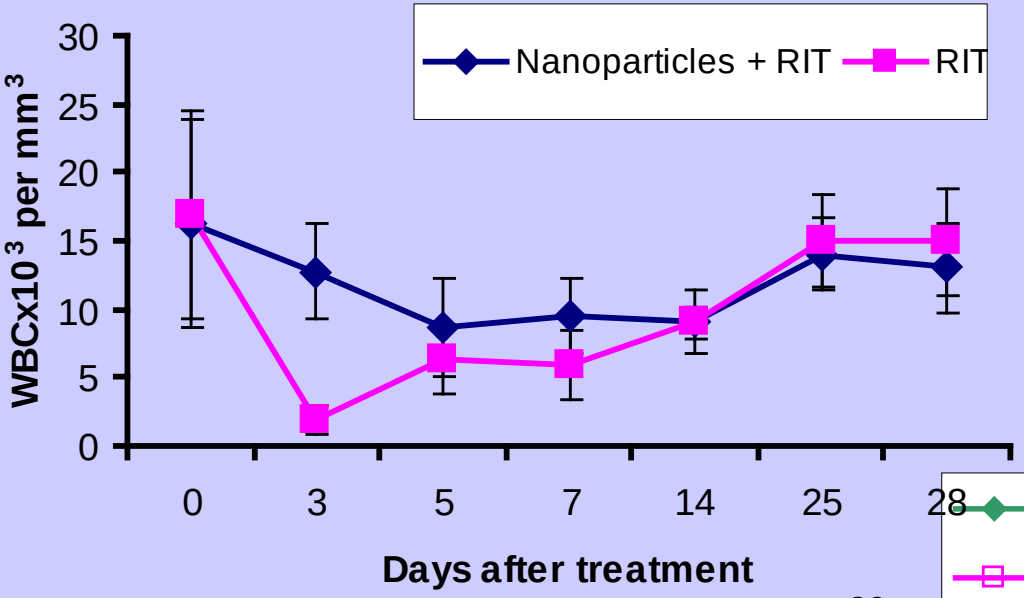
Synthesis and characterization of melanin nanoparticles

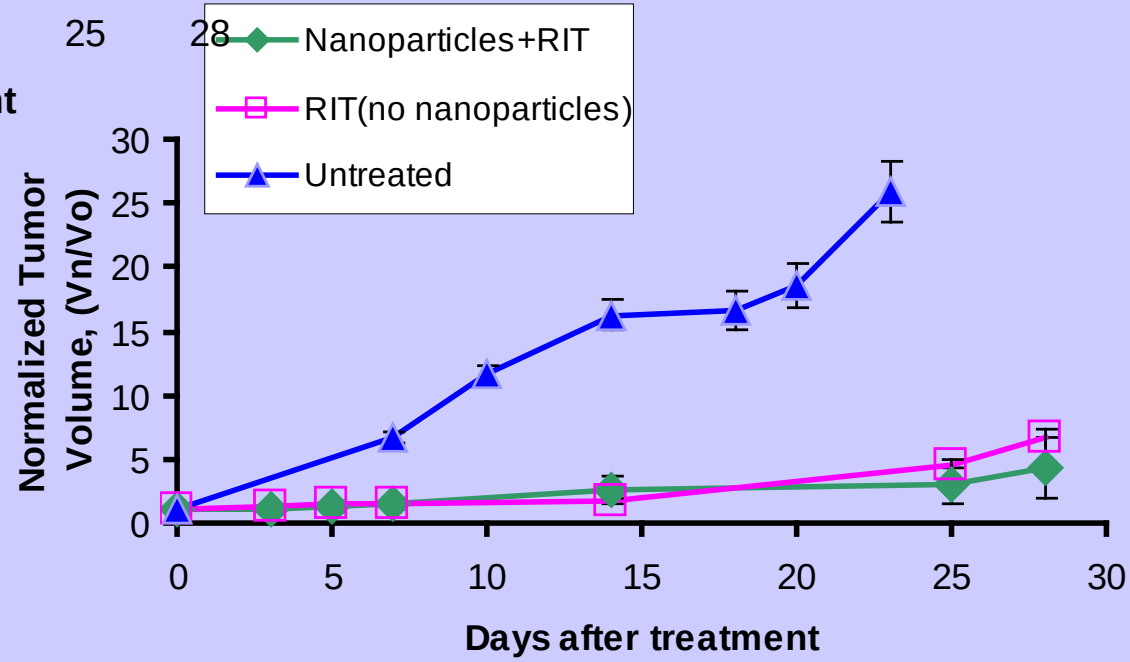






Melanized nanoparticles protect bone marrow in tumor-bearing mice during radioimmunotherapy





Schweitzer AD et al. Int. J. Radiat. Oncol. Biol. Phys. 2010 Apr 24. [Epub ahead of print]

Future plans

- **To synthesize melanin nanoparticles using various combinations of melanin pre-cursors, to extensively characterize them using material science techniques and to investigate the connection between nanoparticles physico-chemical and radioprotective properties.**

- **To evaluate the ability of selected melanin nanoparticles to protect bone marrow from radiation-induced damage during EBRT and RIT.**

- Ruth Bryan
- Xianchun Huang
- Tiffany Moadel
- Andrew Schweitzer
- Phil Aisen
- Robertha Howell
- Josh Nosanchuk